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EXPERIMENTAL STUDIES

Eighteen-Hour Preservation of Rat Hearts With Hexanol and Pyruvate Cardioplegia

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Objectives. **The aim of this study was to evaluate the effectiveness of 1-hexanol as an arresting agent and pyruvate as a substrate in a cardioplegic solution.**

Background. **Heart transplantation is limited in part by the short preservation time of donor hearts. Better preservation techniques would improve patient survival and the time and geographic area for using donor hearts. We previously showed that a cardioplegic solution containing ethanol and pyruvate was superior to a conventional high potassium cardioplegic solution in 24-h cold storage of hamster hearts. Hexanol, a more potent arresting agent than ethanol, might be a more suitable alcohol.**

Methods. **Rat hearts were arrested and stored for 18 h at 4°C with an ethanol (3 vol% = 510 mmol/liter) or 1-hexanol (4 mmol/liter) and pyruvate (10 mmol/liter) cardioplegic solution, St. Thomas' Hospital solution and Stanford solution and subsequently reperfused for 1 h at 35°C. In other groups of hearts, basal oxygen consumption and rest intracellular calcium (Indo 1 technique) were evaluated during ethanol-, hexanol- and potassium-induced cardiac arrest.**

Results. **The percent recovery of left ventricular developed pressure and rate-pressure product were significantly better with the hexanol cardioplegic solution (67 ± 21% and 58 ± 19%, respectively; $p < 0.05$ for all comparisons) compared with the ethanol (10 ± 7% and 5 ± 4%), St. Thomas' Hospital (14 ± 6% and 10 ± 5%) and Stanford solutions (2 ± 2% and 2 ± 1%, respectively). Exclusion of ethanol and hexanol from storage solutions did not influence functional recovery. Values for oxygen consumption after 15- and 30-min ethanol- and hexanol-induced arrest were significantly lower than those after potassium-induced cardiac arrest. There was no difference in the rest intracellular calcium during cardiac arrest induced by the three arresting agents.**

Conclusions. **A hexanol and pyruvate cardioplegic solution was more favorable than ethanol or conventional solutions for long-term cold storage of rat hearts. The beneficial effects of hexanol may have been provided in part by lower energy consumption during hexanol-induced cardiac arrest. These results may have implications for preservation of hearts for heart transplantation.**

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Despite numerous modifications and innovations in preservation techniques, the safe period for clinical heart transplantation is limited to approximately 4 h (1). Data from the Registry of the International Society for Heart Transplantation documented a progressive increase in mortality in the 1st 30 days with increasing ischemic time even within the clinically accepted safe time window (2). Recently, rapid growth in the number of heart transplants reached a plateau because of donor heart availability (3). Thus, better and longer-term cardioplegic solutions would improve patient survival and opportunities for transplantation.

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High concentrations of potassium have been widely used, alone or in combination with other arresting agents (4), to provide diastolic cardiac arrest. High potassium concentrations, however, have possible adverse effects such as vascular endothelial damage (5). It is known that alcohols are potent arresting agents and their acute effects are reversible (6,7). Alcohols potentially scavenge oxygen free radicals (8) and prevent the development of calcium paradox (9). In a previous study (10), we reported that a cardioplegic solution containing ethanol and pyruvate was more effective than a conventional high potassium cardioplegic solution for 24-h cold storage of hamster hearts. The weak cardiac effects of ethanol necessitated use of a high dose. Recently, [^{15}O]butanol was utilized as a tracer for the radiologic measurement of cerebral blood flow in clinical cases (11), showing a possible applicability of longer chain alcohols in humans. These observations led us to evaluate hexanol, which has more potent effects on the heart than does ethanol. We conducted this study to compare the efficacy of ethanol, hexanol and standard high potassium cardioplegic solutions in 18-h cold storage of rat hearts and to characterize

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ethanol-, hexanol- and potassium-induced cardiac arrest by measuring intracellular calcium (Indo 1 technique) and basal oxygen consumption.

Methods

Animals. Sprague-Dawley rats weighing 250 to 300 g were used. Larger rats (350 to 400 g) were used for the surface fluorometry with Indo 1. All animals were treated humanely according to the guidelines of the Animal Research Committee of the University of California, San Francisco.

Isolated heart perfusion. The rats were anesthetized with ether, and the hearts were excised rapidly through a midline sternotomy and perfused within 30 to 60 s by a modified Langendorff method with a perfusion pressure of 140 cm water (7,9,10,12–16). The hearts were perfused with a modified Krebs-Henseleit solution that had the following millimolar composition; sodium chloride (NaCl), 117; potassium chloride (KCl), 5; calcium chloride ($CaCl_2$), 2; magnesium sulfate ($MgSO_4$), 1.2; sodium bicarbonate ($NaHCO_3$), 25; sodium ethylenediaminetetraacetic acid (NaEDTA), 0.5; and glucose, 15. The medium was bubbled with a gas mixture of 95% oxygen and 5% carbon dioxide at 25°C. The temperature was subsequently raised to 35°C to dissolve maximal oxygen in the solution. The oxygen tension of the perfusate was maintained between 550 and 600 mm Hg. All experiments were done after 15 to 20 min of baseline perfusion. The preparation was stable for 2 h with this system.

Physiologic measurements. Myocardial oxygen consumption was calculated as a product of the arteriovenous oxygen difference and coronary flow and was normalized for dry heart weight. Arterial samples were aspirated from the aortic chamber, and venous samples were drawn from a catheter introduced into the right ventricular outflow tract. Oxygen tension of these samples was measured with a Corning model 165/2 gas analyzer (Corning Glassworks). Coronary flow was measured by collecting the right ventricular effluent for 1 min. The dry heart weight was measured after 72-h storage at 110°C. Left ventricular pressure was obtained from a cannula introduced through the left atrial appendage into the left ventricular cavity and connected to a Statham P23Db pressure transducer (Gould) and recorded on a six-channel dynograph (Gould).

Measurements of intracellular calcium by surface fluorometry with Indo 1. Fluorescence excitation was provided by a 100-W mercury vapor lamp. The light was directed through a 365 ± 10 nm discriminating filter and a custom-made silica fiber-optic cable, designed to assess excitation and emission simultaneously, onto a circular area of 38.5 mm^2 of the cardiac surface. The right ventricular free wall was cut out in a circular shape (about 8 mm in diameter), and the tip of the fiber-optic cable was fixed firmly on the right ventricular side of the interventricular septum. In rat hearts, coronary branches supplying the right ventricular free wall arise from and course perpendicular to the proximal main trunk of the right coronary artery and do not supply the left ventricle or the interventricular septum (17). Therefore, creating a hole in the right ventricular free wall does not interfere with left ventricular or septal perfusion. When a large right ventricular branch had to be cut, it was ligated to prevent any coronary steal. Firm contact between the optic fiber and cardiac surface is pertinent to obtain a reliable measurement. Because forceful cardiac compression by the optic fiber could cause changes in the shape of the left ventricle and changes in myocardial perfusion, left ventricular pressure was monitored simultaneously to ensure that the optic fiber did not produce serious hemodynamic derangements. We confirmed that placement of the optic fiber did not change developed pressure by >5% of the control value. Simultaneous monitoring of left ventricular pressure also served to corroborate the hemodynamic effects of interventions. The emitted fluorescence was collected by a coaxial cable of 300-quartz fiber optics, divided by a beam splitter and then filtered at 400 ± 5 and 510 ± 12.5 nm. Output from the photomultiplier tubes at 400 and 510 nm and its ratio (F400/F510), an index of intracellular calcium, were recorded on the six-channel dynograph simultaneously with the left ventricular pressure and the electrocardiogram.

The fluorometer was offset for autofluorescence of the heart before Indo 1 loading. Sixteen milligrams of Indo 1-acetoxymethyl solubilized in dimethylsulfoxide (1 ml) was added to 600 ml of Krebs-Henseleit solution containing 5% calf serum and 3.6 mmol/liter $CaCl_2$. Hearts were perfused with Indo 1 for 45 min at 25°C followed by 30- to 45-min washout. In our previous studies, Indo 1 loading was facilitated by perfusion with a solution containing a high concentration of calcium at a low temperature (13–16).

Although this technique enables us to evaluate changes in intracellular calcium in intact perfused hearts, possible limitations must be considered. The most serious issue associated with the use of cell-permeable form of Indo 1 is sequestration of Indo 1 in the mitochondria, which gives rise to spatial heterogeneity of Indo 1 fluorescence and makes it difficult to estimate a cytosolic calcium level (18). Therefore, we evaluated percent changes of F400/F510 from the control amplitude (difference between peak and trough) of the fluorescence ratio instead of estimating a cytosolic calcium concentration. A problem specific to the whole heart preparation is a contribution of cells other than myocardium, especially endothelium, to Indo 1 fluorescence. In our experimental setting, however, the contribution of endothelium, evaluated by bradykinin administration, is almost negligible (14). When hearts were subjected to zero-flow ischemia, Indo 1 fluorescence transients continued despite rapid contractile cessation (16). This observation implies that fluorescence transients are due not to the cardiac motion but to intracellular calcium oscillation.

Experimental protocol. *18-h cold storage of rat hearts.* After baseline perfusion and physiologic measurements, all hearts were arrested by 1-min perfusion of one of the cardioplegic solutions listed below with a perfusion pressure

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of 80 cm water. One-minute perfusion delivered about 15 ml of cardioplegic solutions to the hearts, which was more than the clinical dose (about 3 ml/g of heart) (19). Takahashi et al. (20) reported that sufficient cardiac protection was achieved by 1-min perfusion of St. Thomas' Hospital solution. All cardioplegic solutions were precooled at 20°C. Osmotic pressures of the cardioplegic solutions were measured with an Advanced Micro-Osmometer model 3MC (Advanced Instruments).

Ethanol cardioplegic solution: This solution had a millimolar composition of NaCl, 115; KCl, 5; $MgSO_4$, 5; $CaCl_2$, 0.5; $NaHCO_3$, 10; potassium phosphate (KH_2PO_4), 1; pyruvate, 10; and 3% (vol/vol = 510 mmol/liter) of ethanol; a pH of 7.3 to 7.4 and osmolarity of 800 mOsm/liter.

Hexanol cardioplegic solution: This solution had the same ionic composition as the ethanol cardioplegic solution except that it contained 4 mmol/liter of 1-hexanol instead of ethanol. It had a pH of 7.3 to 7.4 and osmolarity of 285 mOsm/liter. A preliminary study confirmed that 4 mmol/liter of hexanol was the minimum concentration that could arrest hearts completely under normal physiologic conditions.

St. Thomas' Hospital solution (Plegisol, Abbott): The solution had a millimeter composition of NaCl, 110; KCl, 16; $MgCl_2$, 16; $CaCl_2$, 1.2; and $NaHCO_3$, 10; a pH of 7.8 and osmolarity of 324 mOsm/liter.

Stanford solution: This solution had a composition of 30 mmol/liter KCl, 25 mmol/liter $NaHCO_3$, 5 g/dl glucose and 1.25 g/dl mannitol; a pH of 7.8 and osmolarity of 450 mOsm/liter (4).

After hearts were arrested, the aortic and left ventricular cannulas were disconnected, and the hearts were immersed in 300 ml of the cardioplegic solution at 4°C with which they had been arrested. A cold temperature of 4°C was suitable for long-term storage of hearts (21). During cold storage, both aortic and left ventricular cannulas were maintained open to allow some oxygen diffusion. After 18 h of storage, all hearts were reperfused with Krebs-Henseleit solution for 60 min and recovery of cardiac function was evaluated. For reperfusion, both aortic and left ventricular cannulas were clamped again and placed in position on the perfusion apparatus. The temperature of the perfusate was increased gradually from 25°C to 35°C during the 1st 20 min of reperfusion.

To evaluate whether the presence of ethanol and hexanol in the storage solutions afforded additional protection during cold storage, another group of hearts was studied. In these hearts, arrest with the precooled ethanol or hexanol cardioplegic solution was followed by storage for 18 h at 4°C in a solution that contained no alcohol but had the same ionic composition as the ethanol or hexanol cardioplegic solution. Recovery was evaluated as previously described.

Basal oxygen consumption and rest intracellular calcium during ethanol-, hexanol-, and potassium induced arrest. To characterize ethanol, hexanol and potassium as arresting agents, oxygen consumption and changes in Indo 1 fluorescence were evaluated during perfusion with Krebs-Henseleit solution containing 3% ethanol, 4-mmol/liter 1-hexanol, or 16-mmol/liter potassium at 35°C. In this experiment, Krebs-Henseleit solution was used instead of cardioplegic solutions to explore the pure effects of alcohols and potassium. Oxygen consumption and Indo 1 fluorescence were evaluated in different groups of hearts. Cardiac arrest was maintained for 15 and 30 min for measurements of Indo 1 fluorescence and oxygen consumption, respectively. The $CaCl_2$ concentration of the Krebs-Henseleit solution was reduced to 1.2 mmol/liter in this experiment because 3% ethanol was sometimes insufficient to arrest hearts completely in the presence of a high calcium concentration at physiologic temperature. When ethanol was used to arrest hearts, only hearts that stopped completely were used for data analysis.

Statistical analysis. Values are expressed as mean value ± 1 SD. Differences among groups under corresponding conditions were analyzed by one-factor analysis of variance and Scheffé F test. Changes in indexes from baseline values were evaluated by paired t test or repeated measurement analysis of variance with Scheffé F test. A p value < 0.05 was considered significant. Numbers of animals used for statistical evaluations are described in the tables and figures.

Results

Eighteen-hour cold storage of rat hearts. There was no significant difference in physiologic indexes during baseline perfusion before cold storage among the ethanol, hexanol, St. Thomas' Hospital and Stanford solutions. Mean values of the four groups were 244 ± 44 beats/min for heart rate, 93 ± 5 mm Hg for developed pressure, 22.7 ± 4.3 × 10^3 mm Hg/min for rate-pressure product, 18.9 ± 3.4 ml/min per g wet weight for coronary flow, 36 ± 6 μmol/min per g dry weight for oxygen consumption and 2.7 ± 1.5 mm Hg for left ventricular end-diastolic pressure. Pressure tracings before and after 18-h storage with the four solutions in representative hearts are shown in Figure 1. Left ventricular developed pressure was better preserved with the hexanol solution than with the other three solutions. The percent recovery of physiologic indexes except end-diastolic pressure is shown in Figure 2. All physiologic indexes after 60 min of reperfusion, except heart rate in the hexanol cardioplegic solution, were significantly different from baseline values. However, developed pressure, rate-pressure product and oxygen consumption were significantly better preserved with the hexanol solution (67 ± 21%, 58 ± 19% and 80 ± 27%, respectively) than with the other solutions. Coronary flow was also better preserved with the hexanol solution than with the ethanol and Stanford solutions. Increases in left ventricular end-diastolic pressure were not significantly different among the four cardioplegic solutions.

Recovery of hearts arrested with the ethanol or hexanol cardioplegic solution and stored in the solution without alcohols was the same as that of hearts stored in alcohol-containing solutions (Table 1). Therefore, inclusion of alco-

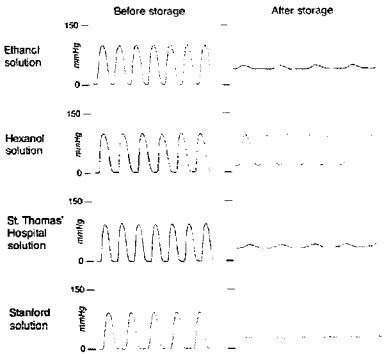


Figure 1. Representative left ventricular pressure tracings before and after 18-h cold storage with the ethanol, hexanol, St. Thomas' Hospital and Stanford solutions. Left ventricular developed pressure was favorably maintained with the hexanol cardioplegic solution.

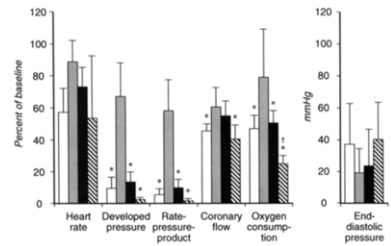
hols in the storage solution was not essential for 18-h cold storage.

Basal oxygen consumption during ethanol-, hexanol- and potassium-induced cardiac arrest. There was no difference in physiologic indexes among the three groups during the control period. Values for left ventricular end-diastolic pressure at 30 min of cardiac arrest were the same for all three groups (32 ± 20, 38 ± 22 and 31 ± 20 mm Hg for ethanol-, hexanol- and potassium-induced arrest, respectively). Coronary flow at 30 min of arrest by ethanol (12 ± 2 ml/min per g wet weight) was significantly lower than that in hexanol- and potassium-induced arrest (19 ± 3 and 18 ± 4 ml/min per g wet weight, respectively).

Oxygen consumption values after the control period and at 15 and 30 min of cardiac arrest are depicted in Figure 3. Basal oxygen consumption became stable within 15 min of arrest, and values at 30 min of arrest were not significantly different from those at 15 min in all groups. At both 15 and 30 min of arrest, the basal oxygen consumption with potassium-induced arrest was significantly higher by ≈20% than with either ethanol- or hexanol-induced arrest.

Changes in Indo 1 fluorescence during ethanol-, hexanol- and potassium-induced cardiac arrest. Intracellular calcium may play an important role in regulating oxygen utilization (15,22). As oxygen consumption became stable within 15 min of cardiac arrest, a group of hearts was subjected to 15 min of arrest and changes in Indo 1 fluorescence were evaluated. Figure 4 shows representative changes in the F400/F510 ratio. All agents decreased both systolic and diastolic F400/F510 ratios rapidly and the transients discontinued within 3 min. Rest F400/F510 ratios after discontinuation of transients remained stable during 15 min of arrest in all groups. Values for rest F400/F510 ratio at 5, 10 and 15 min of arrest, expressed as percent changes of the baseline amplitude of F400/F510 transients from the baseline diastolic level, are summarized in Table 2. There was no difference in rest F400/F510 ratios among the three arresting agents.

Figure 2. Percent recovery of physiologic indexes and increases in end-diastolic pressure after 18-h cold storage of 28 rat hearts. Values are mean value ± 1 SD. □ = ethanol solution (n = 7); ▨ = hexanol solution (n = 7); ■ = St. Thomas' Hospital solution (n = 7); ▧ = Stanford solution (n = 7). *$p < 0.05$ versus hexanol solution. †$p < 0.05$ versus St. Thomas' Hospital solution. The hexanol cardioplegic solution preserved left ventricular developed pressure, rate-pressure product and oxygen consumption significantly better than did the other three solutions.



Discussion

Hexanol and pyruvate as potentially effective components in cardioplegia. This study was designed to test whether cardioplegia and storage with a newly developed hexanol and pyruvate solution would provide better long-term cardiac preservation, compared with that of St. Thomas' Hospital and Stanford solutions and a previously evaluated experimental ethanol cardioplegic solution (10). St. Thomas' Hospital solution has an extracellular-type composition similar to the alcohol solutions, and its clinical efficacy has been confirmed in routine cardiac operations (23). To improve the outcome of long-term cold storage, several modifications of cardioplegic solutions have been made, among which the use of the intracellular-type ionic composition and prevention of cellular edema by osmotic and oncotic agents are considered to be most promising (19,24). Stanford solution is a prototype of the intracellular-type solution with mannitol and glucose as osmotic agents and has been used extensively for clinical heart transplantation (4,19,24). In nonperfused rat hearts, cold storage with crystalloid cardioplegic solutions has been limited to a maximal duration of 12 h to allow for sufficient recovery (21,25). Poor recovery after storage with St. Thomas' Hospital and Stanford solutions supports these observations. However, with the hexanol cardioplegic solu-

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Table 1. Percent Recovery of Physiologic Indexes and Increases in End-Diastolic Pressure After 18-Hour Storage of Rat Hearts in the Storage Solution Without Alcohols

Cardioplegic Solution	Heart Rate (%)	Developed Pressure (%)	Rate-Pressure Product (%)	Coronary Flow (%)	Oxygen Consumption (%)	End-Diastolic Pressure (mm Hg)
Ethanol (n = 7)	51 ± 14	16 ± 1.	5.5 ± 3	45 ± 20	45 ± 12	39 ± 24
Hexanol (n = 7)	83 ± 17	65 ± 19	55 ± 16	67 ± 15	78 ± 16	20 ± 15

These values (mean ± 1 SD) were not significantly different from values in hearts stored in solutions containing alcohols.

tion, hearts recovered developed pressure and rate-pressure product to 67% and 58%, respectively, after 18 h of cold storage. These observations indicate that the hexanol and pyruvate solution may be more suitable for long-term cardiac preservation than are conventional solutions. A comparison between ethanol and hexanol solutions clearly showed the superiority of hexanol to ethanol.

Several previous studies addressed the problems of storage solutions, because diffusion of water and components of the solutions into the myocardium during long-term storage may influence the formation of cell edema and the efficacy of cardioplegic solutions (21,25). Therefore, we evaluated the significance of alcohols in the storage solution. Omitting alcohols from the storage solution did not affect functional recovery after 18 h of cold storage. This observation suggests that alcohols may be retained in the cardiac tissue through their high partitioning to the lipid bilayer (26,27) even if alcohols are absent from the storage solution.

Beneficial mechanisms of hexanol and pyruvate. High concentrations of potassium reduce the resting membrane potential (28,29), inactivating the sodium channel and thereby causing cardiac arrest (29). Ethanol and hexanol bring about cardiac arrest probably through modifications of intracellular calcium metabolism (30–32) and direct inactivation of the sodium channel, as evidenced in nerves (33) and possibly in myocardium (31,34). It was reported that basal oxygen consumption during cardiac arrest induced by tetrodotoxin was 20% lower than that in potassium-induced arrest (35). Consistent with this observation, ethanol and hexanol reduced basal oxygen consumption by about 20% from the level achieved with potassium. A lower oxygen requirement possibly reduces the energy expenditure used to maintain cellular integrity during cold storage, thus prolonging an effective preservation time. There is a good correlation between intracellular calcium and oxygen consumption (15). Calcium regulation of enzymes of the Krebs cycle may be a key regulatory mechanism of mitochondrial oxidative phosphorylation (22). On the basis of these concepts, we measured rest levels of intracellular calcium during ethanol-, hexanol- and potassium-induced arrest. However, there was no difference among the three agents. Alcohols are known to depress the sarcolemmal sodium pump function and calcium

Figure 3. Oxygen consumption (mean value ± 1 SD) during the control period and after 15 and 30 min of ethanol-, hexanol- and potassium-induced cardiac arrest in 19 rats. □ = ethanol arrest (n = 5), ▨ = hexanol arrest (n = 7) and ■ = potassium arrest (n = 7). *p < 0.05 versus ethanol and hexanol arrest. Values for oxygen consumption at both 15 and 30 min of ethanol- and hexanol-induced arrest were significantly lower than for potassium-induced arrest.

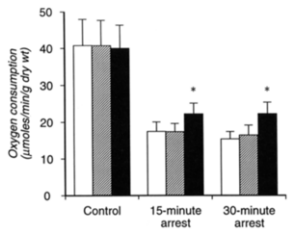

Figure 4. Representative tracings of Indo 1 fluorescence ratios (F400/F510) during ethanol (A), hexanol (B) and potassium perfusion (C). Perfusion with these agents decreased both systolic and diastolic fluorescence ratios rapidly and fluorescence transients disappeared within 3 min of perfusion. The rest fluorescence ratio was stable during a 15-min observation period for all agents. The time scale is for the slow recording speed.

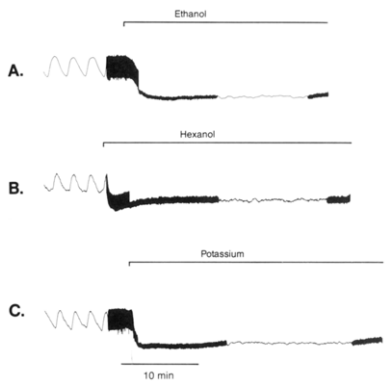

Table 2. Rest Indo 1 Fluorescence Ratio (F400/F510) During Ethanol-, Hexanol- and Potassium-Induced Cardiac Arrest

Arresting Agents	Arrest Period		
	5-Min	10-Min	15 Min
Ethanol (n = 8)	−78 ± 20	−79 ± 18	−70 ± 22
Hexanol (n = 10)	−78 ± 21	−75 ± 21	−72 ± 21
Potassium (n = 8)	−81 ± 19	−80 ± 18	−74 ± 15

All values differed significantly ($p < 0.05$) from baseline diastolic levels. Values are expressed as mean value ± SD and represent changes from baseline diastolic fluorescence ratio, expressed as percent of baseline amplitude of fluorescence transients. There was no difference in the rest fluorescent ratio among the three groups.

uptake by sarcoplasmic reticulum (36,37), both of which are energy-requiring biochemical processes. These effects of alcohols may have contributed to the low basal energy expenditure. Oxygen radical scavenging effects of low doses of alcohol (8) and prevention of calcium paradox (9) might be other beneficial mechanisms.

The ethanol and hexanol cardioplegic solutions contained 10 mmol/liter of pyruvate as a substrate to augment energy production. In a previous study in rats, pyruvate retarded high energy phosphate depletion and acidosis during 30 min of regional ischemia and thus enhanced functional and metabolic recovery during reperfusion (12). It appeared that pyruvate was an effective supplementary factor in a cardioplegic solution, probably augmenting oxidative energy production (10). Glucose and fatty acids are not suitable for this purpose because a buildup of by-products including sugar phosphates is deleterious to the ischemic heart (13).

A high concentration of ethanol in the ethanol cardioplegic solution possibly made it less useful for long-term preservation of rat hearts. Several previous studies suggested intracellular sites of ethanol action (30,31,36), indicating that ethanol could penetrate into cells easily. A high intracellular ethanol content might cause cell edema, especially during reperfusion. The effects of ethanol on the cell membrane may also have contributed to the poor recovery, because concentrations of ethanol >500 mmol/liter cause lipid peroxidation (38).

Limitations of the study. Several issues remain to be evaluated concerning the use of hexanol in cardioplegic solutions. Even if all hexanol contained in the stored heart enters the systemic circulation during reperfusion, a blood concentration of hexanol would be much lower than anesthetic concentrations tested in animals (39). In a baboon study, a small amount of hexanol (about 10 mmol) was injected into the carotid artery as a radiologic tracer for a cerebral blood flow measurement without any significant adverse effects (40). Hexanol is metabolized by the liver enzyme alcohol dehydrogenase (41). However, hexanol has not been used for clinical purposes and the short term adverse effects of hexanol in humans are not known. Procedures for transplanting the stored heart to a recipient allow hexanol to be vented out through the right atrium while the coronary vascular bed is replaced with blood from the aorta. This would prevent the entry of a large amount of hexanol into the systemic circulation.

The outcome of experimental cardiac preservation depends in part on the animal species used for evaluation (42). Therefore, the beneficial effects of the hexanol solution need to be confirmed in other animal species. Appropriate ionic compositions and additional protection by inclusion of other potentially effective agents and their interaction with hexanol must also be elucidated.

Conclusions. An experimental cardioplegic solution containing 4-mmol/liter 1-hexanol and 10-mmol/liter pyruvate provided better protection during 18-h cold storage of rat hearts than did conventional potassium solutions, thus suggesting a new approach for long-term cardioplegic preservation. Lower basal energy consumption during hexanol arrest may be a beneficial mechanism. Further evaluation of hexanol cardioplegia is warranted.

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